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Preventive Veterinary Medicine

journal homepage: www.elsevier.com/locate/prevetmed



Factors related to longevity and mortality of dogs in Italy

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ARTICLE INFO

Keywords: Animal welfare Cause of death Dog Epidemiology Lifespan

ABSTRACT

Besides its translational value, an improved understanding of dog longevity and mortality is necessary to guide health management decisions, breed selection, and improve dog welfare. In order to analyse the lifespan of dogs in Italy, identify the most common causes of death, and evaluate possible risk factors, anonymised medical records were collected from 9 veterinary teaching hospitals and 2 public health institutions. Data regarding breed, sex, neuter status, age, diagnosis, and mechanism of death were retrieved. Cause of death (COD) was classified by pathophysiologic process (PP) and organ system (OS). Of the 4957 dogs that died between 2004 and 2020 included in the study, 2920 (59.0%) were purebred, 2293 (46.2%) were female, 3005 (60.6%) were intact, 2883 (58.2%) were euthanised. Overall median longevity was 10.0 years. Median longevity was significantly longer for crossbreds, females, neutered dogs, and small-sized breeds. The breeds with the highest median age at death were the Yorkshire terrier, English cocker spaniel, West Highland white terrier, Italian volpino, and Shih Tzu, whilst the American bulldog, English bulldog, American pit bull terrier, Bernese mountain dog and the Maremma and the Abruzzes sheepdog had the lowest median age at death. The most frequent COD by PP was neoplasia (34.0%), which occurred more frequently in large breeds, namely German shepherd, Labrador retriever and Boxer. Degenerative diseases mostly affected small-sized dogs like Miniature pinscher and Dachshund. Regarding the OS involved, diseases of the renal/urinary system were most frequently responsible for COD (15.0%). prevalently degenerative and inflammatory/infectious. Substantial variation in median longevity according to causes of death by PP and OS was observed. These data are relevant for breeders, veterinary practitioners, and owners, to assist breed selection, facilitate early diagnosis, guide choice when purchasing a purebred dog and making health management decisions, and ultimately improve dog welfare.

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1. Introduction

Dogs are the first domesticated animals and have been living alongside humans for thousands of years (Perri, 2016). Unlike laboratory animals, they share the same environment, risk factors, exposure to pathogens, and habits with humans. Moreover, the dog's genome shows greater sequence similarity to the human's than the mouse's, and many canine diseases display the same genetic basis, clinical presentation, progression, or response to treatment as the corresponding human diseases (Parker et al., 2010; Gilmore and Greer, 2015). All these aspects render the dog a unique model for human spontaneous diseases and ageing (Mazzatenta et al., 2017).

Due to the long and intense selection processes it was subjected, the modern domestic dog exhibits exceptional phenotypic variability with 356 FCI-recognised breeds (www.fci.be). However, over the years, the intensive selection of key desirable traits has led to a severe reduction of breed genetic variability and the unintentional amplification of negative characteristics (Gray et al., 2009). As a result, breed-specific diseases such as cancer, cardiovascular diseases, and autoimmune disorders have become more frequent (Ostrander et al., 2000; Patterson, 2000). Dog size and breed have been shown to influence longevity and causes of death (Fleming et al., 2011; O'Neill et al., 2013; Lewis et al., 2018).

Besides its translational value, an improved understanding of dog longevity and mortality represents an important opportunity for breeders, veterinary practitioners, and owners, to assist breed selection, facilitate early diagnosis, guide choice when purchasing a purebred dog and making health management decisions, and ultimately to improve dog welfare.

Dog health monitoring and medical care expenses are second only to that of humans (AVMA, 2022). Many data sources are available for canine health surveillance, including veterinary clinical records, pet insurance databases, and questionnaire-based surveys, each of them carrying different strengths and weaknesses (O'Neill et al., 2014).

Several country-specific studies investigating dog longevity and cause of death have been published (Michell, 1999; Egenvall et al., 2000; Proschowsky et al., 2003; Bonnett et al., 2005; Fleming et al., 2011; O'Neill et al., 2013; Inoue et al., 2015; Huang et al., 2017; Lewis et al., 2018). To the authors' knowledge, data on the Italian dog population are not available.

The objective of this study was to analyse the lifespan of dogs in Italy, to identify the most common causes of death, and to evaluate possible associations between risk factors such as sex, neuter status, breed, size, and longevity, by analysing a database of combined clinical records from veterinary hospitals and public health institutions located throughout Italy. Besides its national relevance, this study is of global interest as it sheds light on the risk factors related to disease and longevity, and on breeds affected by a worryingly short life expectancy.

2. Materials and methods

Anonymised medical records were collected from the digital database of 9 Veterinary Teaching Hospitals (University of Bologna - UNIBO, University of Messina - UNIME, University of Naples - UNINA, University of Padua - UNIPD, University of Parma - UNIPR, University of Perugia - UNIPG, University of Pisa - UNIPI, University of Teramo -UNITE, University of Turin - UNITO) and 2 public health institutions (Istituto Zooprofilattico Sperimentale dell'Abruzzo e del Molise "Giuseppe Caporale" - IZSAM, Istituto Zooprofilattico Sperimentale della Lombardia e dell'Emilia-Romagna "Bruno Ubertini" - IZSLER). Experimental Zooprophylactic Institutes (IZSs) operate as technical-scientific bodies of the National Health Service. Among their numerous functions, their mission to monitor and improve animal health is carried out by performing epidemiologic surveillance and diagnosis of animal diseases and zoonoses. Data regarding breed, sex, neuter status, age, diagnosis (clinical and/or anatomopathological), and mechanism of death (natural, euthanasia, fatal accident) were retrieved. The study was approved by the Ethical Committee of the University of Bologna (Approval number, 204868; Approval date, 24 July 2023).

The dataset was checked and harmonised in Microsoft Excel (Microsoft Corporation, 2018). Breed names were aligned by using the English version of the FCI breeds' nomenclature (www.fci.be); the American Kennel Club nomenclature was used for non-FCI recognised breeds (www.akc.org). Sex and neuter status were combined to create a sex/neuter variable (intact male, neutered male, intact female, spayed female). Based on the weight range reported for adults in published standards, breeds were classified according to size as small (\leq 10 kg), medium (11–25 kg), large (26–45 kg) and giant (>45 kg) (Grandjean and Haymann, 2004). Mixed-breed dogs were evaluated as a single group and excluded from the size analyses.

When multiple diagnoses were reported in one record, a single cause of death (COD) was identified, whenever possible, as the disease encompassing all or most of the other descriptive or symptomatic diagnoses, or the disease that was most likely to have caused death due to its severity, and for neoplasia the site of the primary tumour. Only confirmed diagnoses were considered. Each COD was then classified by pathophysiologic process (PP) and organ system (OS) involved (cardiovascular, dermatological, endocrine, gastrointestinal, hematopoietic, hepatic, musculoskeletal, neurological, renal/urinary, reproductive, respiratory, systemic). The 10 PP categories were: congenital, degenerative, idiopathic, infectious, inflammatory (including immunemediated), metabolic, neoplastic, toxic, traumatic, and vascular. Dubious cases were discussed among the authors and a decision was made upon a consensus. COD was classified by PP and OS based on the founding textbooks of internal medicine (Ettinger et al., 2017) and pathology (Grant, 2016). Whenever it was not possible to classify the COD by either PP or OS, a designation of "undetermined" was used. Non-confirmed diagnoses were classified as "undetermined".

2.1. Statistical analysis

Statistical analysis was conducted using R Core Team (2021). Breed-specific analyses were limited to those breeds with \geq 20 representatives. A P < 0.05 was considered significant. Overall, longevities were calculated using median, interquartile range (IQR) and range. Differences in median longevity between purebred and crossbred, male and female (overall and within breeds with \geq 20 representatives), intact and neutered/spayed dogs, were investigated using the U Mann-Whitney test. To test for differences in longevity according to mechanism of death, sex and neuter status and among breeds of different sizes, the Kruskal-Wallis test was used for overall comparison. Whenever significant, the Dunn's test with Bonferroni correction for multiple comparisons was applied.

Percentage frequencies of deaths attributable to each PP and OS within a given age, size, or breed (with $\geq \! 20$ representatives) were calculated.

To investigate the possible influence of sex and neuter status on COD, significant differences in PP frequencies in the different groups (intact female, spayed female, intact male, neutered male) were checked by using a chi-squared test followed by Fisher's exact test for post hoc analysis.

When the sample dimension allowed it, significant differences between within-breed proportional mortality (WBPM) and overall proportional mortality (OPM) by PP were investigated by using a Bayesian approach and applying a beta distribution model. Specifically, differences were considered significant when the 95% confidence intervals of the WBPM and OPM for the considered PP did not overlap.

3. Results

Overall, 4957 dogs that died between 2004 and 2020 were included in the study (Appendix: Supplementary Table S1), of which 2037 (41.0%) were crossbred and 2920 (59.0%) were purebred, including 904

small (30.9%), 691 medium (23.7%), 1252 large (42.9%), and 73 giant (2.5%) size dogs. In total, there were 139 breeds, of which 39 were represented by ≥ 20 dogs (n = 4474); apart from crossbreds, the most numerous were German shepherd (n = 287), Labrador retriever (n = 287) 214), Boxer (n = 137), Golden retriever (n = 109) and English setter (n = 109) 100). As regards sex/neuter status, 2060 dogs (41.6%) were intact males, 481 (9.7%) were neutered males, 87 (1.8%) were males with unknown neuter status, 941 (19.0%) were intact females, 1300 (26.2%) were spayed females, 52 (1.0%) were females with unknown neuter status; information on sex and neuter status was not available in 36 (0.7%) cases. Sex was equally distributed in all age groups, with a slight prevalence of males (Appendix: Supplementary Fig. S1). Mechanism of death was euthanasia in 2883 cases (58.2%), natural death in 1593 (32.1%) cases, fatal accident in 388 (7.8%) cases, and unknown in 93 (1.9%) cases. In 181 (3.6%) cases. COD was classified as undetermined for both PP and OS; 392 (7.9%) cases could not be classified for PP and 181 (3.6%) cases could not be classified for OS (Appendix: Supplementary Table S2).

Overall, longevity was similarly distributed in purebred and crossbred dogs (Fig. 1). The median longevity of the overall dog population was 10.0 years (IQR 7.0–13.0; range 0.0–26.0). The median longevity for crossbreds (11 years; IQR 7.0–14.0; range 0.0–20.0) was greater than for purebreds (10 years; IQR 6.0–12.0; range 0.0–26.0; P <0.0001). Table 1 shows breed-specific longevities (median, IQR and range) for breeds with \geq 20 representatives. The breeds with the highest median age at death were the Yorkshire terrier, English cocker spaniel, West Highland white terrier, Italian volpino, and Shih Tzu; whereas the American bulldog, English bulldog, American pit bull terrier, Bernese mountain dog and the Maremma and the Abruzzes sheepdog showed the lowest median age at death.

Median longevity was significantly different among purebred dogs of different sizes (P < 0.001), with small breeds living longer than larger breeds (Table 2). Females (n = 2293; median 10 years; IQR 7.0–13.0; range 0.0–23.0) lived longer than males (n = 2628; median 10 years; IQR 6.0–13.0; range 0.0–24.0; P < 0.0001) (Appendix: Supplementary Fig. S2). At breed level, the greater median longevity of females compared with males was statistically significant in Dogo argentino, Italian volpino, and in mixed-breed dogs (P < 0.05) (Appendix: Supplementary Fig. S3).

Neutered/spayed dogs lived longer than intact dogs; in particular, spayed females (11 years; IQR 8.0–14.0; range 0.0–21.0) lived longer than intact females (9 years; IQR 5.0–13.0; range 0.0–23.0; P < 0.0001) and intact males (10 years; IQR 6.0–13.0; range 0.0–21.0; P < 0.0001), and neutered males (11 years; IQR 8.0–13.0; range 1.0–24.0) lived longer than intact males (P < 0.0001) and intact females (P < 0.0001) (Fig. 2).

Significant differences in longevity according to the mechanism of death were also observed. Specifically, the differences in longevity between dogs dying by euthanasia (median 11 years; IQR 8.0-13.0; range

Table 1 Longevity of dog breeds with \geq 20 representatives (n=39). The median, interquartile range (IQR), range for the age (years) at death and number of dogs included are shown. Breeds are listed from the highest median age at death to the lowest.

Breed	Median	IQR	Range	Dogs (n)
Yorkshire terrier	13.0	10.0–14.0	0.0-24.0	67
English cocker spaniel	13.0	10.0–14.0	0.0-26.0	61
West Highland white terrier	13.0	11.0–15.0	0.0-17.0	37
Italian volpino	12.5	9.5–15.0	5.0-21.0	20
Shih Tzu	12.5	10.0–14.0	1.0-17.0	44
Poodle (Miniature)	12.0	9.5–14.0	5.0–17.0	47
Poodle (Toy)	12.0	1.0 - 15.0	0.0 - 18.0	45
Dachshund	11.5	9.0-13.0	1.0-18.0	92
Mixed-breed	11.0	7.0-14.0	0.0-20.0	2037
Labrador retriever	11.0	7.0 - 13.0	0.0 - 16.0	214
Pinscher (Miniature)	11.0	7.8-14.0	0.0-21.0	82
Beagle	11.0	6.8 - 13.3	0.0 - 19.0	77
Maltese	11.0	8.8-14.0	0.0 - 18.0	73
Pug	11.0	8.0-14.0	1.0-16.0	41
Romagna water dog	11.0	5.5-14.0	0.0-18.0	40
Pomeranian	10.5	7.8-14.0	1.0-19.0	20
German shepherd	10.0	7.0-12.0	0.0 - 18.0	287
Golden retriever	10.0	8.0-13.0	0.0-17.0	109
English setter	10.0	7.0-13.0	0.0-17.1	100
Cavalier King Charles spaniel	10.0	8.0-11.8	1.0-16.0	62
Brittany spaniel	10.0	9.0-13.0	0.0 - 19.0	41
German shorthaired pointing dog	10.0	7.5-12.0	0.0-14.0	27
English springer spaniel	9.5	6.3-14.0	0.0-16.0	34
Boxer	9.0	6.0 - 11.0	0.0-20.0	137
Rottweiler	9.0	6.0 - 11.0	0.0-15.0	74
Italian cane corso	9.0	6.0 - 11.0	0.0-16.0	54
Border collie	9.0	4.0-12.5	0.0-18.0	48
Pointer	9.0	6.0 - 12.8	1.0-16.0	22
Chihuahua	8.5	3.0-12.0	0.0-17.0	60
Jack Russell terrier	8.0	5.0-12.8	0.0 - 18.0	66
Dobermann	8.0	5.0-10.5	0.0-14.0	59
French bulldog	8.0	5.0-10.0	0.0-14.0	46
Italian segugio	8.0	3.0-10.5	0.0 - 15.0	41
American Staffordshire terrier	8.0	4.0-12.0	0.0-17.0	33
Maremma and the Abruzzes sheepdog	7.5	4.0–11.0	0.0–14.0	55
Bernese mountain dog	7.0	5.0-8.8	0.0-14.0	43
American pit bull terrier	7.0	3.5–11.8	0.0–17.0	21
English bulldog	6.0	3.0-9.0	0.0-14.0	33
American bulldog	5.0	2.0–10.5	0.0-13.0	25

0.0–24.0), natural death (median 9 years; IQR 6.0–12.0; range 0.0–23.0) and fatal accident (median 7 years; IQR 3.0–11.0; range 0.0–26.0) were statistically significant between all the compared pairs (P < 0.0001).

Overall, the most frequent COD by PP was neoplasia (34.0%), followed by degenerative and inflammatory diseases (Table 3). Neoplasia involving the hematopoietic system was by far the most frequent (29.1%) (Supplementary Table S2). While being the leading COD in dogs of all sizes, neoplasia occurred more frequently in large dog breeds,

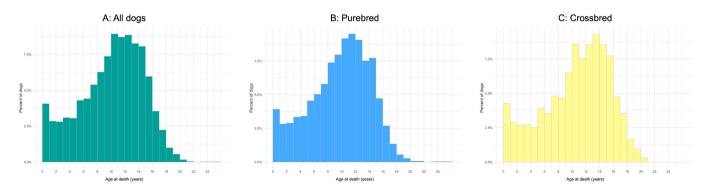


Fig. 1. Percentage distribution for age at death of the dogs included in the study, showed in 2-year age bands. A: all dogs (n = 4957); B: purebred dogs (n = 2920); C: crossbred dogs (n = 2037).

Table 2 Longevity of purebred dogs according to size (n = 2920). The median, interquartile range (IQR), range for the age (years) at death and number of dogs are shown.

Size	Median	IQR	Range	Dogs (n)
Small	11.0 ^a	8.0-14.0	0.0-24.0	904
Medium	10.0^{b}	6.0-13.0	0.0-26.0	691
Large	9.0°	6.0-12.0	0.0-20.0	1252
Giant	7.0^{d}	4.0-9.0	0.0-13.0	73

Superscripts indicate the results of the Kruskall-Wallis test followed by Dunn's multiple comparison test with sequential Bonferroni adjustment. Median longevities without a common superscript differ (P < 0.001).

whereas degenerative and metabolic diseases mostly affected smallsized dogs. Infectious diseases were more frequent in medium-sized dogs, and giant breeds showed a higher recurrence of disease of vascular origin (e.g., Gastric Dilation/Volvulus) (Appendix: Supplementary Fig. S4). Significantly different frequencies in COD by pathophysiologic process according to sex and neuter status were found; namely, higher frequency of infectious and traumatic diseases in intact dogs, lower frequency of inflammatory diseases in intact females contrarily to spayed females, higher frequency of neoplastic diseases in spayed females contrarily to intact males (Table 4). Supplementary Table S3 shows the percentage of deaths within each PP category and the main PP COD for breeds with >20 representatives. Neoplasia was the leading COD in most breeds; the five most affected were Rottweiler (52.7%), Boxer (46.0%), English cocker spaniel (46.0%), miniature Poodle (42.6%) and Italian cane corso (40.7%). Degenerative diseases affected mostly the Cavalier King Charles spaniel (51.6%), followed by toy Poodle (35.6%), Chihuahua (33.3%), Dobermann (32.2%) and Maltese (31.5%). Inflammatory (including immune-mediated) diseases were the main COD of the Italian volpino (35.0%) and English bulldog (21.2%). The breeds with the highest relative frequency of infectious diseases as COD were the German short-haired pointing dog (29.6%), Italian segugio (29.3%), and American pit bull terrier (23%). Fig. 3 illustrates significantly higher (red) and lower (green) within-breed proportional mortality (WBPM) by PP compared to the overall proportional

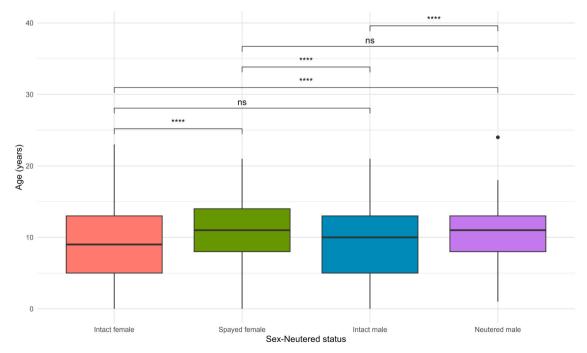
Table 3Longevity according to cause of death by pathophysiologic process (in order of frequency). The median, interquartile range (IQR), range for the age (years) at death and number and percentage of dogs are shown. The undetermined causes of death are shown but not considered when ranking the causes of death.

Pathophysiologic Process	Median	IQR	Range	Dogs (%)
Neoplastic	11.0	9.0-13.0	0.0-24.0	1493 (34.0)
Degenerative	11.0	9.0-14.0	0.0 - 20.0	804 (18.3)
Inflammatory	9.0	6.0-12.0	0.0-23.0	673 (15.4)
Infectious	6.0	1.0-10.0	0.0-17.0	522 (11.9)
Traumatic	6.0	3.0-12.0	0.0 - 26.0	432 (9.9)
Vascular	10.0	7.0-13.0	0.0 - 18.0	218 (5.0)
Metabolic	12.0	7.0-13.0	0.0 - 18.0	92 (2.1)
Toxic	6.5	3.0-11.0	0.0 - 19.0	73 (1.7)
Congenital	2.0	0.0 – 6.0	0.0-14.0	57 (1.3)
Idiopathic	7.0	5.0-11.3	0.0 - 16.0	20 (0.5)
Undetermined	11.0	7.0-14.0	0.0 - 19.0	573

 $\label{thm:condition} \begin{tabular}{l} \textbf{Table 4} \\ \textbf{Increased and decreased frequencies in COD by pathophysiologic process according to sex and neuter status (Fisher's exact test) (n = 4243). Undetermined causes of death were excluded from the analysis. \\ \end{tabular}$

Pathophysiologic	Sex and neuter status			
Process	Intact female	Spayed female	Intact male	Neutered male
Congenital Degenerative Idiopathic Infectious Inflammatory	↑*** ↓*** ↑ns ↑**** ↓**	↓ ns ↓ ns ↓ ns ↓ ****	↓ ^{ns} ↑ ^{ns} ↑ ^{ns} ↑ ^{ns} ↑* ↓ ^{ns}	↓* ↑ ns ↓ ns ↓ ns ↓ ns ↑ ns
Metabolic Neoplastic Toxic Traumatic Vascular	↓ ns ↓ ns ↓ ns ↑ *** ↑ ns	↑ns ↑**** ↓ns ↓**** ↑ns	\frac{ns}{****} \tag{ns} \tag{ns} \tag{ns} \tag{ns}	\(\begin{align*} al

Signification codes: ns P >0.05; * P $\leq\!0.05;$ ** P $\leq\!0.01;$ *** P $\leq\!0.001;$ **** P $\leq\!0.0001.$



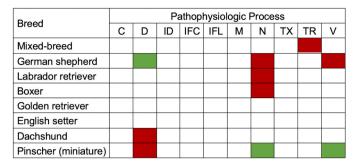


Fig. 3. Significant differences in proportional mortality by pathophysiologic process among the most numerous breeds compared to the overall dog population (P < 0.05). Significantly higher within-breed proportional mortality (WBPM) is shown in red, and significantly lower WBPM is shown in green. C – Congenital; D – Degenerative; ID – Idiopathic; IFC – Infectious; IFL – Inflammatory; M – Metabolic; N – Neoplastic; TX – Toxic; TR – Traumatic; V – Vascular. Undetermined causes of death were not considered.

mortality (OPM) of the sampled dog population, calculated for the most numerous breeds. For example, German shepherds, Labrador retrievers and Boxers had a higher WBPM due to neoplasia. Conversely, miniature Pinscher had a lower WBPM due to neoplasia and vascular diseases, and a higher WBPM due to degenerative diseases, along with the Dachshund.

Diseases of the renal/urinary system were most frequently responsible for COD (15.0%), followed by gastrointestinal, cardiovascular, hematopoietic, and neurological diseases (Table 5). Medium-sized dogs were the most affected by renal/urinary disorders, whilst gastrointestinal diseases occurred most frequently in giant breeds. Cardiovascular diseases were more prevalent in small-sized dogs, whereas hematopoietic disorders prevailed in large-sized dogs (Appendix: Supplementary Fig. S5). Supplementary Table S4 shows the percentage of deaths within each OS category and the main OS COD for breeds with >20 representatives. The breeds with the highest relative proportion of cardiovascular causes of death were the Cavalier King Charles spaniel (53.2%) and Chihuahua (33.3%). Gastrointestinal diseases were the leading COD in American pit bull terrier (33.3%), Italian segugio (22.0%), German shepherd dog (19.9%), Italian cane corso (18.5%), English pointer (18.2%) and Maremma and the Abruzzes sheepdog (16.4%). The breeds most affected by hematopoietic disorders were the Bernese mountain dog (23.3%), Rottweiler (21.6%), Golden retriever (20.2%), and English cocker spaniel (18.0%). Neurological diseases were the leading COD in Romagna water dogs (22.5%), Boxers (19.7%) and Yorkshire terriers (14.9%). Renal/urinary diseases as COD occurred most commonly in Brittany spaniel (29.3%), Italian volpino (25.0%), Beagle (24.7%), American Staffordshire terrier (21.2%) and English springer spaniel (20.6%). The highest relative frequency of respiratory diseases was

Table 5
Longevity according to cause of death by organ system (in order of frequency). The median, interquartile range (IQR), range for the age (years) at death and number and percentage of dogs are shown. The undetermined causes of death are shown but not considered when ranking the causes of death.

Organ System	Median	IQR	Range	Dogs (%)
Renal/urinary	10.0	6.0-13.0	0.0-20.0	688 (15.0)
Gastrointestinal	8.0	3.0-12.0	0.0-26.0	625 (13.6)
Cardiovascular	11.0	8.0-14.0	0.0 - 20.0	564 (12.3)
Hematopoietic	10.0	7.0-13.0	0.0 - 20.0	539 (11.7)
Neurological	11.0	6.0-14.0	0.0 - 20.0	505 (11.0)
Systemic	8.0	3.0-12.0	0.0 - 19.0	402 (8.8)
Respiratory	11.0	8.0-13.0	0.0 - 23.0	348 (7.6)
Musculoskeletal	10.0	5.0-13.0	0.0 - 19.0	308 (6.7)
Hepatic	11.0	8.0-14.0	0.0 - 19.0	225 (4.9)
Endocrine	12.0	9.3-14.0	0.0-24.0	167 (3.6)
Reproductive	12.0	9.0-13.0	1.0-19.0	158 (3.4)
Dermatological	12.0	10.0-14.0	3.0-21.0	66 (1.4)
Undetermined	11.0	8.0-13.0	0.0-19.0	362

observed in the West Highland white terrier (27.0%), English bulldog (24.2%) and Pug (22.0%).

Figs. 4 and 5 show the age distribution of the different causes of death within PP and OS classifications, respectively. Congenital, infectious, traumatic, toxic and, to some extent, inflammatory diseases tended to occur earlier in life, determining a shortening of the dog's lifespan. Conversely, dogs that reached an older age were more often affected by degenerative, metabolic and neoplastic processes, with neoplasia showing a marked peak at 12 years of age (Fig. 4A). Regarding OSs, diseases involving the gastrointestinal, neurological, musculoskeletal, renal/urinary system and systemic were relatively frequent in younger dogs, albeit increasing again at older ages. On the other side, the cardiovascular, endocrine, hematopoietic, reproductive, and respiratory systems were progressively involved as the dogs aged, peaking around 12 years (Fig. 5).

4. Discussion

This study of over five thousand dogs provides up-to-date information on longevity and causes of death in Italian dogs.

Dog life expectancy appears to have increased over the years, perhaps due to the advances in veterinary medicine, the growing interest in animal welfare, and the increased willingness and availability of owners to pay for their pet's care. Early studies carried out in the United States between the '70 s and the '80 s recorded a lifespan ranging between 6 and 8 years (Bronson, 1982; Patronek et al., 1997). In this study, the overall median longevity was 10.0 years, which is in line with what has been reported in studies carried out on German (Eichelberg and Seine, 1996), Danish (Proschowsky et al., 2003), Taiwanese (Huang et al., 2017), and British dogs (Lewis et al., 2018), but slightly shorter than other estimates of the British dog population, obtained through surveys and electronic patient records from primary veterinary practices (Michell, 1999; Adams et al., 2010; O'Neill et al., 2013).

In general, crossbreds lived 1.0 year longer than purebred dogs, as also observed in other studies (Patronek et al., 1997; Proschowsky et al., 2003; O'Neill et al., 2013; Huang et al., 2017). This finding can be explained by the inbreeding phenomena that likely affect purebred dogs, which more often carry homozygous deleterious genes, and by hybrid vigour (Yordy et al., 2020). However, there was wide variation in longevity across breeds, with some purebreds living longer than mixed-breed dogs. The breeds with a high median age at death (over 12.5 years) were the Yorkshire terrier, English cocker spaniel, West Highland white terrier, Italian volpino, and Shih Tzu, all small-sized breeds. Indeed, although among mammals larger species generally live longer than smaller species (Galis et al., 2007), within the dog species an inverse correlation between longevity and body size, with small breeds living longer than larger breeds, has been observed, in agreement with previous studies (Li et al., 1996; Patronek et al., 1997; Michell, 1999; Proschowsky et al., 2003; Galis et al., 2007; Greer et al., 2007; Adams et al., 2010; Fleming et al., 2011; O'Neill et al., 2013; Huang et al., 2017; Lewis et al., 2018). This difference in longevity according to size has been credited to artificial selection, leading to accelerated growth, earlier senescence onset, and pathological conditions (Patronek et al., 1997; Hawthorne et al., 2004; Urfer et al., 2007; Kraus et al., 2013). In our study, dogs of larger breeds were more frequently affected by neoplastic diseases, whereas small-breed dogs died more frequently from degenerative and metabolic disorders. However, further studies are needed to better identify the biological mechanisms underlying the ageing process (Selman et al., 2013).

The breeds with a low median age at death are also worth some reflection. Besides large breed dogs (Bernese mountain dog, Maremma and the Abruzzes sheepdog), bull-type terriers and brachycephalic breeds, including the American bulldog, English bulldog, American pit bull terrier, American Staffordshire terrier and French bulldog, had the shortest lifespan. Indeed, brachycephalic breeds are susceptible to several early-onset diseases, including spinal disease and brachycephalic

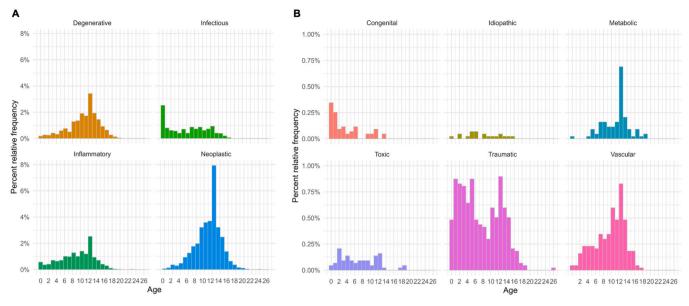


Fig. 4. Percentage relative frequency of causes of death by pathophysiologic process (PP) as a function of age (years) for all dogs (n = 4384, excluding 573 individuals with undetermined PP). A: PPs with higher percentage relative frequencies; B: PPs with lower percentage relative frequencies.

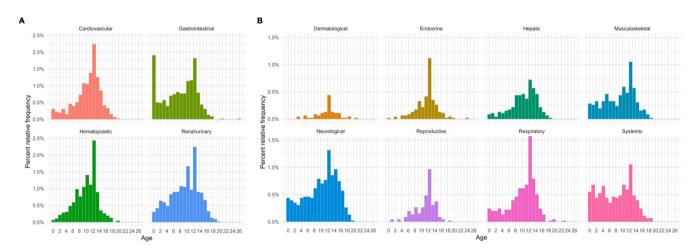


Fig. 5. Percentage relative frequency of causes of death by organ system (OS) as a function of age (years) for all dogs (n = 4595, excluding 362 individuals with undetermined OS). A: OSs with higher percentage relative frequencies; B: OSs with lower percentage relative frequencies.

obstructive airway syndrome, that impair their life expectancy (Gough et al., 2018).

Other factors influencing dog longevity were sex and neuter status. Females lived longer than males, and neutered/spayed dogs lived longer than intact dogs, regardless of sex. No significant differences were observed between males and females with the same neuter status. Previous studies have shown similar, although not always identical, results (Bronson, 1982; Michell, 1999; Egenvall et al., 2000; O'Neill et al., 2013; Huang et al., 2017). This suggests that neuter status affects longevity more than sex itself (Hoffman et al., 2018). Due to the nature of our data, dogs were dichotomously classified as neutered or intact based on their gonadal status at the time of death. However, it has been demonstrated that failing to take into consideration lifetime gonadal hormone exposure can lead to inaccurate assumptions regarding the relationship between neuter status and longevity, particularly for female subjects (Waters et al., 2011). Moreover, since neutering/spaying is frequently regarded as a stand-in for responsible dog ownership and better care, neutered/spayed dogs' lifespan may benefit from improved owner care (Diesel et al., 2010). Therefore, these results should be interpreted with caution.

Most of the dogs in our study were euthanised (58.2%), reflecting a growing concern amongst dog owners for quality of life over its length. However, although euthanasia is an artificial termination of life, the median longevity of euthanised dogs was significantly longer than that of dogs that died a natural death (11.0 vs. 9.0 years). This might as well be a sign of responsible ownership, resulting in improved healthcare for the dog.

Consistent with other studies, neoplasia was by far the most frequent COD overall (Bronson, 1982; Eichelberg and Seine, 1996; Michell, 1999; Bonnett et al., 2005; Adams et al., 2010; Fleming et al., 2011; O'Neill et al., 2013; Inoue et al., 2015; Huang et al., 2017) and the leading COD in most breeds, including mixed-breed dogs. This indicates that cancer aetiology is multifactorial and, although genetics are important, other factors (e.g., environmental, hormonal) are likely to play a key role in the development of certain tumours and make dogs particularly interesting as models for human oncology (Garden et al., 2018). Nevertheless, some breeds appear to be particularly prone to cancer; significantly higher proportional mortality due to neoplasia was found in German shepherds, Labrador retrievers and Boxers, as previously reported (Craig, 2001; Fleming et al., 2011; Dobson, 2013; Gough et al., 2018).

Contrarily, a significantly decreased risk was observed in miniature Pinscher, which is in turn more susceptible to degenerative diseases, together with the Dachshund. The Cavalier King Charles spaniel and Chihuahua also showed the highest relative proportion of degenerative cardiovascular causes of death. Small and toy breeds are in fact at elevated risk for myxomatous mitral valve disease, i.e., the most commonly diagnosed cardiovascular disease in dogs (Parker and Kilroy-Glynn, 2012; Mattin et al., 2015).

As regards the OS involved, diseases of the renal/urinary system were most frequently responsible for the COD, and prevalently associated with degenerative and inflammatory/infectious diseases. Mediumsized dogs were primarily affected by renal/urinary diseases of infectious aetiology. This is compatible with the high prevalence of working and hunting breeds among medium-sized dogs (e.g., Border collie, English setter, Italian segugio, Brittany spaniel, English springer spaniel, etc.), which are more likely to get in contact with parasitic, bacterial or viral pathogens (e.g., Leishmania infantum, Leptospira spp., Parvovirus) during their activities.

COD significantly differed also according to sex and neuter status. In both sexes, neutering was associated with an increased frequency of neoplastic and inflammatory (including immune-mediated) diseases, which were significantly higher in spayed females. Indeed, neutering has been associated with an increased risk of cancers including osteosarcoma, mast cell tumour, lymphoma, and hemangiosarcoma (Oberbauer et al., 2019) and a greater prevalence of immune disorders (Sundburg et al., 2016). Besides the prevention of reproductive disorders, neutering is performed to reduce aggressive behaviour, biting, and roaming (Gershman et al., 1994; Maarschalkerweerd et al., 1997; Neilson et al., 1997). Although more recently the effectiveness of gonadectomy in preventing aggressive and roaming behaviour has been questioned (Farhoody et al., 2018; Roulaux et al., 2023), in our study population intact dogs showed a significantly higher frequency of traumatic (e.g., hit-by-car, bite injuries) and infectious diseases, in line with previous studies (Hoffman et al., 2013). This might be related to specific canine behaviours, intrinsic risk factors (e.g., puppies and young dogs being more at risk of parvovirosis) but also differences in veterinary care or in dog management and lifestyle, since working and hunting dogs are more commonly intact. Lastly, female dogs showed a lower frequency of degenerative diseases, namely of the cardiovascular system, which was significantly reduced in intact females. Previous studies have reported higher odds of diagnosed degenerative mitral valve disease in male dogs (Serfass et al., 2006; Mattin et al., 2015). These results highlight the need to further investigate the complex relationship between cause of death and gonadal status.

Finally, the present study highlighted substantial variation in median longevity according to causes of death by PP and OS. As could be expected, congenital, infectious, toxic and traumatic diseases – frequently involving the gastrointestinal, neurological and musculoskeletal systems – were associated with a shorter lifespan. Conversely, dogs that reached an older age were more often affected by degenerative, metabolic and neoplastic processes – affecting the cardiovascular, endocrine, hematopoietic and reproductive systems. Illnesses that are likely to have long, painful and/or debilitating courses should raise welfare concerns, since living a long life does not necessarily mean that it is a life worth living. Therefore, ensuring an adequate "quality of life" should be a priority for both dog owners and veterinary practitioners.

Studies on dog longevity and COD have been carried out using different data sources. Questionnaire-based surveys are relatively inexpensive and feasible, but they are affected by response rate and validation issues, recall and non-responder bias (Adams et al., 2010). Pet insurance databases can provide a lot of information, but their representativeness of the general population is questionable due to variable coverage among breeds and age, and loss of data regarding low-cost or excluded disorders (Egenvall et al., 2009). Veterinary clinical records benefit from better diagnostic reliability and generalisability, and record digitisation has made large amounts of data easy to retrieve and analyse

(Fleming et al., 2011; O'Neill et al., 2013). In our study, only records with a confirmed diagnosis were used. However, there were some limitations. Our data included only patient visits at veterinary teaching hospitals that eventually resulted in death and necropsy reports from public health institutions. Firstly, this may tend to bias our results, including dogs with more complicated or severe diseases, or with owners more concerned with their health or willing to pay. Health insurance for dogs is in fact hardly taken out in Italy. Secondly, the entire at-risk dog population was not known, and data were not captured for dogs that did not receive veterinary care; therefore, the conclusions drawn from these data cannot be generalised to characterise the risk of mortality among dogs overall. Lastly, since breed identity was provided by the owner and a pedigree check was not performed, it cannot be excluded that some dogs were misclassified by breed or were crossbreds strongly resembling purebred dogs. However, since the majority of dogs were registered as mixed-breed, this suggests that most of them had been classified correctly.

5. Conclusions

To our knowledge, this is the first large-scale retrospective study on dog mortality in Italy. The overall median longevity of dogs accessing veterinary teaching hospitals or public health institutions and dying between 2001 and 2020 is 10.0 years. Mixed-breed dogs generally live longer than purebreds, but there is significant variation in median longevity across breeds. Dog size is inversely correlated to longevity. Neutering/spaying appears to be positively related to longevity, although an improved understanding of the relationship between gonadal status and cause of death is needed. Neoplasia is the most frequent cause of death, mostly affecting large-sized dogs. Our results suggest that the primary focus should shift from mere life expectancy to an in-depth investigation of causes of death, to help identify priority diseases in specific breeds, capitalise the efforts to improve breed health, and assist owners in purchasing a purebred dog and making health management or end-of-life decisions. Furthermore, given the similarity of numerous canine and human diseases, an improved understanding of the epidemiologic factors related to dog longevity and mortality carries an invaluable translational value that deserves to be further explored.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

Carlo Guglielmini: Investigation, Writing - review & editing. **Eleonora Gori:** Data curation, Investigation, Writing – review & editing. Giovanni L. Alborali: Investigation, Writing - review & editing. Maurizio Dondi: Investigation, Writing - review & editing. Sara Rota Nodari: Investigation, Writing - review & editing. Paolo E. Crisi: Data curation, Investigation, Writing - review & editing. Sonia Sabatelli: Data curation, Investigation, Writing - review & editing. Annamaria Conte: Formal analysis, Investigation, Methodology, Writing - review & editing. Francesco Porciello: Investigation, Writing – review & editing. Paola Gianella: Investigation, Writing - review & editing. Micaela Sgorbini: Investigation, Writing - review & editing. Annamaria Passantino: Investigation, Writing - review & editing. Romolo Salini: Formal analysis, Methodology, Visualization, Writing - review & editing. Marco Pietra: Conceptualization, Investigation, Methodology, Writing - review & editing. Angelo Peli: Conceptualization, Formal analysis, Methodology, Resources, Supervision, Writing - review & editing. Paolo Dalla Villa: Investigation, Writing - review & editing. Michele Podaliri: Data curation, Investigation, Writing - review & editing. Paolo Ciaramella: Investigation, Writing - review & editing. Cristina Di Palma: Investigation, Writing - review & editing. Mariana **Roccaro:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft.

Declaration of Competing Interest

We have no conflicts of interest to disclose and we did not receive any financial support.

Acknowledgements

We would like to thank Prof. Andrea Boari and Susanna Tora for their valuable contribution to the manuscript.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.prevetmed.2024.106155.

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